Prevention of Sudden Cardiac Death: a Probabilistic Model for Decision Support

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ABSTRACT

As part of the Cardiac Arrhythmia and Risk of Death Patient Outcomes Research Team (CARD PORT) study we are developing a comprehensive decision model to help physicians identify preferred strategies for preventing sudden cardiac death. The model integrates three components: a screening model, a treatment model, and a value model. Ultimately this model will use the CARD PORT's collective findings to produce policy recommendations and will support patient-specific clinical decision making. Our initial modeling suggests the importance of patient-specific value models in an analysis of treatment options. Although our model is specific to cardiac sudden death, other medical domains that exhibit similar characteristics – the importance of patient preferences and the uncertainty regarding the benefits of strategies for risk stratification and treatment – can use a conceptual framework similar to the approach we used to represent strategies to prevent sudden cardiac death..

INTRODUCTION

Sudden cardiac death accounts for half of the 700,000 cardiac deaths each year in the United States. Despite intensive investigation, physicians are uncertain about both who is at risk for sudden cardiac death and how best to treat those patients they believe are at risk. Although many tests are available that may stratify patients into risk categories, their value is unproven currently. In addition, physicians and patients have a choice between several drug therapies and implantable cardiac defibrillators (ICD), which sense electrical abnormalities and deliver a shock to the heart to restore normal rhythm.

The medical benefits and attendant risks of these therapies have not been directly compared, although several ongoing randomized trials are attempting to address this issue. Preliminary results from one trial suggest that there is no overall mortality benefit of ICD over drug [1]. Given the uncertainty of treatment effect and the importance of considering patient preferences (especially when the medical outcomes between therapies is small), decision modeling can play an important role in informing both broad policy decisions and providing patient-specific clinical decision support.

The Cardiac Arrhythmia and Risk of Death Patient Outcomes Research Team (CARD PORT) is a five-year, multi-institutional study of strategies to prevent sudden cardiac death. The CARD PORT will (1) evaluate screening methods used in populations at risk for sudden cardiac death, and (2) compare the medical effectiveness of alternative treatment strategies for the prevention of sudden cardiac death. The mortality, morbidity, functional status, quality of life, and cost associated with each treatment strategy will be assessed. Ultimately the CARD PORT will build a foundation for clinical policy recommendations for the management of patients at risk for sudden cardiac death. As part of the CARD PORT investigation, we are developing a comprehensive decision model that will integrate the study's collective findings to produce such policy recommendations and will support patient-specific clinical decision making. In this paper, we describe the overall design of the CARD PORT decision model, our implementation of the treatment model, and our plans for future development.

METHODS

The final decision model will incorporate three conceptual components: a screening model, a treatment model, and a value model (Figure 1). Each of these components will integrate the relevant findings from other projects in the CARD PORT study. The screening model will use diagnostic tests and clinical risk factors to estimate (1) the rate of arrhythmic events, (2) likelihood of surviving arrhythmic events, (3) the rate of nonarrhythmic cardiac death, and (4) likelihood of response to drug therapies. The treatment model, which is described in detail below, compares the expected outcomes of drug and device therapy in a variety of clinical outcomes. The value model will incorporate patient specific information concerning risk attitudes and quality of life, as well as an assessment of individual and

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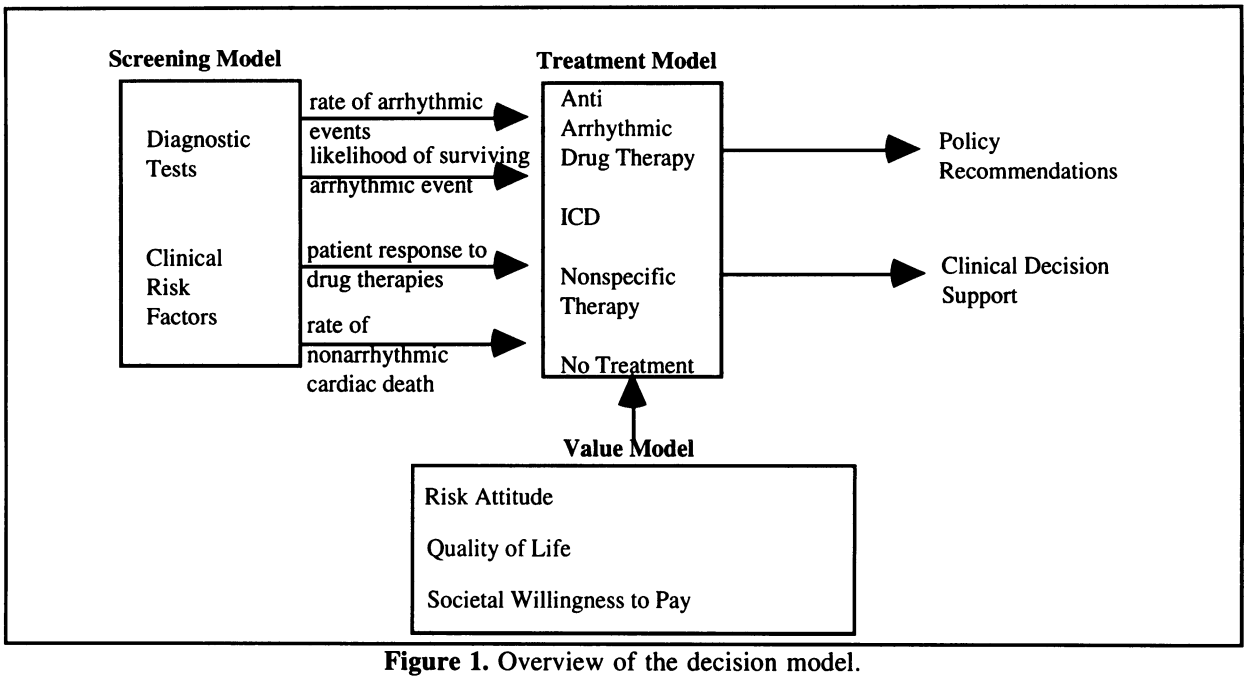

Figure 1. Overview of the decision model.

society's willingness to pay for various treatment alternatives. The screening and value models provide input to the treatment model, permitting us to develop policy recommendations and to support patient-specific clinical decisions. The treatment model is central to our efforts, allowing the user to calculate the life expectancy, quality-adjusted life expectancy, and costs for patients on differing therapies. We will now describe the structure of the model in some detail, and use hypothetical input data to illustrate how the model works.

Modeling Assumptions

We made the following assumptions:

- Patients have an underlying constant baseline rate of arrhythmic events
- ICD decreases the chance of arrhythmic death associated with ventricular tachycardia and ventricular fibrillation as compared to the baseline rate.
- Drug therapy (such as amiodarone or sotolal) decreases the patient's rate of arrhythmic events

Treatment Model Structure

The treatment model is a 13-state Markov model (Figure 2), which we developed to compare the efficacy of pharmalogic therapy to treatment with an ICD. We chose a Markov model because it allowed us to model events as they change over time, such as the risk of ventricular arrhythmias and the risk of noncardiac mortality. The cycle length for the Markov model is one month.

The model has five possible initial treatments. These include ICD, drug (e.g., amiodarone), combination drug and ICD, nonspecific treatment (e.g., aspirin, angiotensin converting enzyme inhibitors), and no treatment.

Table 1 Annual probabilities used in treatment submodel

Treatment	Probability of first arrhythmic event	Probability of further arrhythmic events	Probability of initial NAD	Probability of NAD given prior arrhythmic event	Probability of arrhythmic death given VT	Probability of arrhythmic death given VF	Probability of NI given VT	Probability of NI given VF
No treatment	.20	.25	.09	.15	.60	.95	.020	.15
Non specific	.15	.20	.06	.10	.60	.95	.020	.15
ICD	.15	.20	.06	.10	.02	.05	.005	.02
Drug	.10	.15	.06	.10	.40	.95	.010	.10
ICD and Drug	.10	.15	.06	.10	.02	.05	.005	.02

NAD = Non Arrhythmic Cardiac Death, NI = Neurological Impairment

Each month, patients may experience the following events: ventricular tachycardia (VT), ventricular fibrillation (VF), noncardiac death, nonarrhythmic cardiac death (e.g., myocardial infarction), or no event. Patients who do not have an arrhythmic event, and who do not die within the month cycle, continue on their present treatment. However, if a patient experiences either VT or VF, there are three possible outcomes: an arrhythmic death, survival in a neurologically impaired state, or survival without neurological impairment. Patients who survive an arrhythmic event are then still vulnerable to the risk of noncardiac and nonarrhythmic cardiac death for the remaining portion of the month cycle. If they survive the cycle they are then either kept on their initial treatment choice or switched to another treatment. Patients who become neurologically impaired are immediately switched to a nonspecific treatment and continue on this treatment indefinitely.

Treatment Model Inputs

The population considered in this paper are patients at high risk of recurrence of life threatening ventricular arrhythmias, such as those who previously survived an episode of ventricular tachycardia or fibrillation. The input data used are based on expert judgments of the CARD PORT investigators and will be updated and refined based on a quantitative synthesis of the literature as well as ongoing clinical trials. Patients in the model are 55 years of age. We assume that patients' quality of life is equally and substantially decreased across all therapies (a utility of .75 on a scale from 0 (instant death) to 1 (perfect health)). (Table 1).

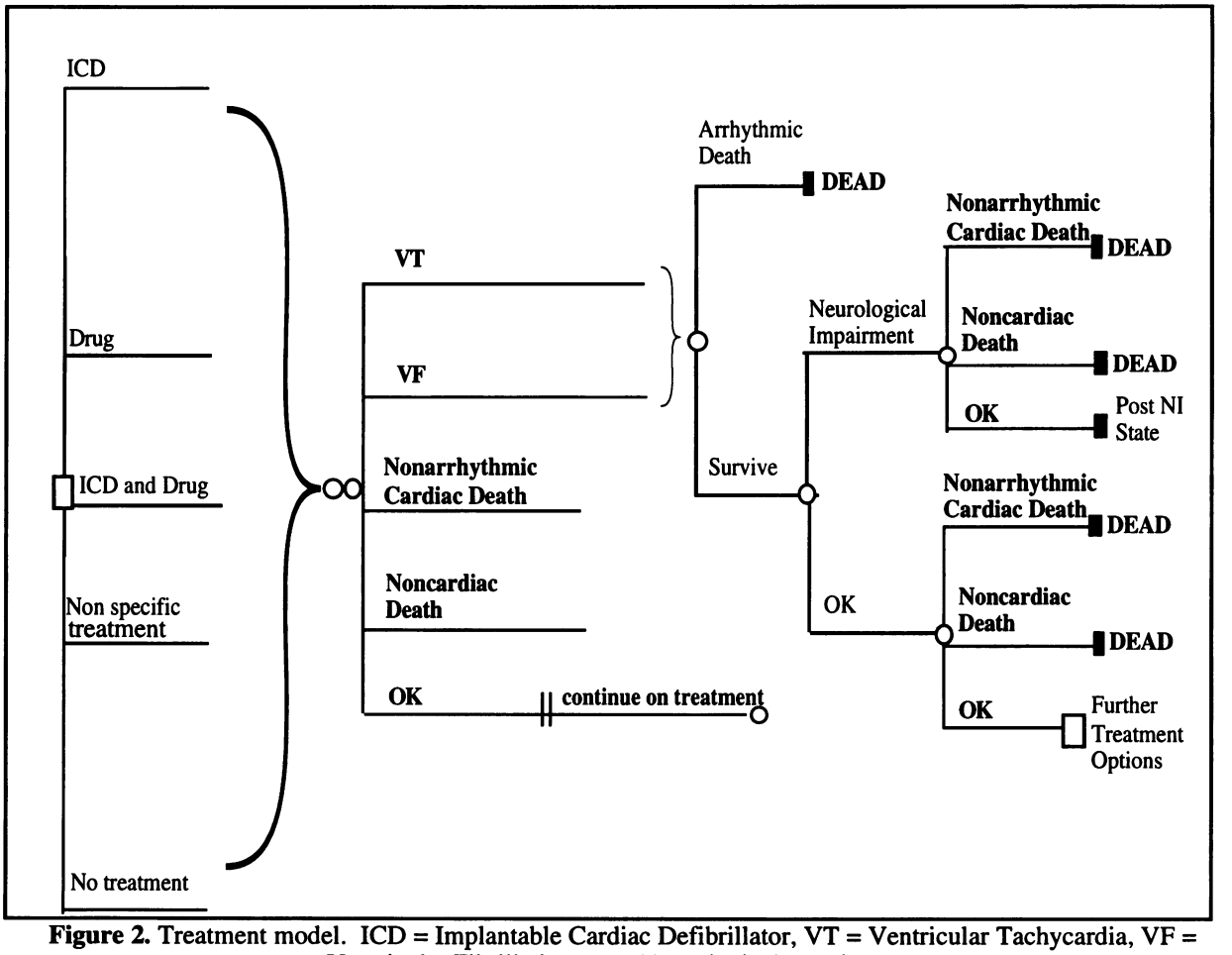

Figure 2. Treatment model. ICD = Implantable Cardiac Defibrillator, VT = Ventricular Tachycardia, VF = Ventricular Fibrillation, NI = Neurological Impairment.

RESULTS

Table 2 shows the quality-adjusted life expectancies (QALE) for patients on the five initial therapies. The combined therapy of ICD and drug has greater expected life years than the other therapies since it both lowers the rate of arrhythmic events (through the presence of the drug) and the reduces the rate of arrhythmic death given a VT or VF (due to the use of the ICD). ICD yielded a QALE 1.95 years more than drug treatment alone.

Table 2. Quality-adjusted life expectancy for treatment strategies.

Treatment	QALE (years)
ICD and Drug	7.10
ICD	6.69
Drug	4.74
Nonspecific	3.60
No treatment	2.62

Figure 3 shows the probability of arrhythmic death given VT/VF on ICD therapy against the probability of an arrhythmic event on drug therapy. For drug therapy to be preferred to ICD, the likelihood of arrhythmic death on ICD must be increased by ten - fold. Note that the graph only depicts probabilities of an arrhythmic event given drug therapy ranging from 0 to 0.2 since above this range ICD is always the preferred treatment strategy given our inputs.

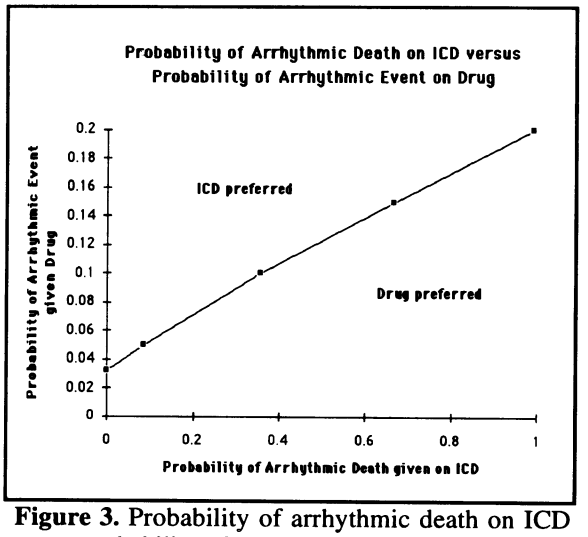

Figure 3. Probability of arrhythmic death on ICD vs. probability of an arrhythmic event on drug therapy.

Figure 4 shows the effect that a patient's utilities for therapy with drugs and ICD has on the preferred therapy. Although our current model favors ICD over drug therapy, this graph shows how the patient utilities for these two therapies could change the quality-adjusted life expectancies of the treatments. For example, drug treatment becomes the preferred strategy when the utility for drug therapy is 0.6 and the utility for ICD is 0.3. These two graphs demonstrate that the model's recommended treatment strategy will be dependent on the inputs from both the screening and value models.

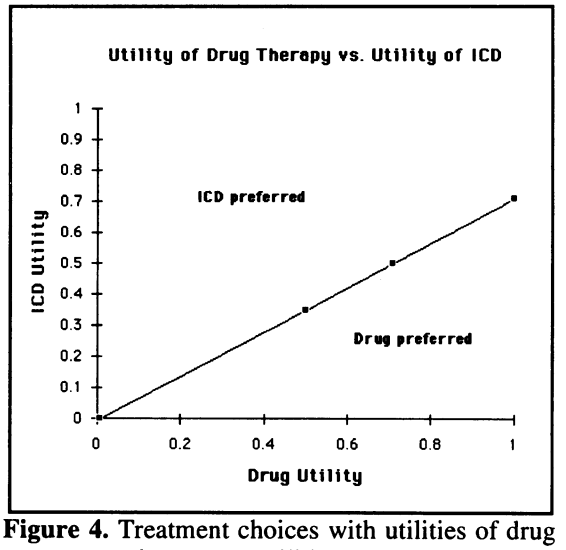

Figure 4. Treatment choices with utilities of drug therapy vs. utilities of ICD.

DISCUSSION

The goal of the CARD PORT study is to provide a scientific foundation for clinical decision making regarding strategies to prevent sudden cardiac death. The entire project will address several important clinical questions, such as determining optimal approaches to risk stratification and assessing various treatment options in terms of medical outcomes, patient preferences, and costs. In this paper, we have described the conceptual framework and initial implementation of the decision model that we will use to develop clinical policies, and to provide patient-specific decision support. In addition, we provided an illustrative example that suggests the importance of patient-specific value models in an analysis of treatment options.

The clinical management of patients at risk for sudden cardiac death presents unique challenges for the development of computer-based decision support.

First, there are many alternative evaluation strategies for risk stratification — including tests of ischemia (e.g., exercise treadmill), tests of left ventricular function (e.g., echocardiogram, radionuclide ventriculography), and tests for abnormal electrical activity (e.g., Holter monitoring, signal-averaged ECGs) — that may be used in combination or sequentially. The most appropriate diagnostic strategy may depend on the patient's underlying disease (e.g., ischemic heart disease), so a decision support system must incorporate this relevant information. Second, a number of competing treatment strategies are available, each with a particular set of risks and uncertainties. Modeling each of the available therapies is complex, and the candidate therapies frequently change. The rapid evolution of information about the efficacy of therapeutic options indicates that a mechanism for systematically updating the probabilistic information and structure of the decision model is needed. Third, cardiac arrhythmias occur unpredictably over a long time horizon, a factor that precludes simple tree-based analyses. Finally, because the treatment options affect quality of life and short-term mortality differently, a comprehensive analysis of treatment options requires a sophisticated value model. These challenges led us to develop conceptually distinct but interrelated submodels, as shown in Figure 1. Although our approach does not provide solutions for all of these problems, it enabled us to simplify and modularize development of the decision model.

To provide patient-specific decision support, the model must incorporate a variety of factors specific to the individual patient. These factors include the presence of co-morbid conditions, the underlying rate of arryhthmic events, the likelihood of surviving an arrhythmic event, the likelihood of response to specific drug therapies, the rate of non-arrhythmic cardiac death, and patients' preferences. Patient preferences include preferences regarding quality of life and attitude about risk taking (i.e., risk preference).

Our analysis was presented as an example only – the inputs for the decision model are currently based primarily on expert judgment – since efficacy data from ongoing randomized trials are not yet available. The example, however, illustrates the potential importance of patient preferences. Although our example shows a 1.95 year quality-adjusted life expectancy difference between therapy with drug versus ICD, this difference is diminished when the quality of life with an ICD is substantially lower than the quality of life with drug therapy. The therapeutic benefit of ICD relative to drug therapy is unlikely to be as large as our example indicates. Randomized clinical trials, now in progress for several years, have presumably not shown marked survival benefits, since early termination has not been judged necessary. Thus, rather small differences in patients' preferences could change optimal treatment decisions. Because patient preferences are likely to vary substantially, we believe there is a role for patient-specific clinical decision support in the domain of treatment for prevention of sudden cardiac death.

The clinical management questions the CARD PORT will highlight a more general problem: When can investigators develop recommendations applicable to a group of patients? conversely, when should recommendations be individualized for each specific patient? A need for patient-specific decision support is suggested by the importance of patient preferences and the uncertainty regarding the benefits of risk stratification and treatment. In general, when the variation in preferences (or other important patient characteristics) within a group of patients is greater than the variation between groups of patients, patient-specific decision support is likely to be useful. To model other medical domains that exhibit these characteristics, analysts can use a conceptual framework similar to the approach we used to represent strategies to prevent sudden cardiac death.

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